| L Number | Hits | Search Text | DB | Time stamp |
|----------|--------------|---|-------------|-------------------|
| 1 | 15 | "rna polymerase" same (mutation or error) | USPAT; | 2003/10/29 12:31 |
| _ | | near3 induc\$5 | US-PGPUB; | |
| 0 | | | DERWENT | |
| 2 | 810 | ("rna polymerase" same (mutation or | USPAT; | 2003/10/29 12:41 |
| | | error)) and (evolution or evolve or | US-PGPUB; | |
| 1 | | selection) | DERWENT | |
| 3 | 2 | (("rna polymerase" same (mutation or | USPAT; | 2003/10/29 12:47 |
| | _ | error)) and (evolution or evolve or | US-PGPUB; | |
| | | selection)) and gold.in. | DERWENT | |
| 4 | 1 | "in vitro" near2 evolution and gold.in. | USPAT; | 2003/10/29 12:37 |
| 1 | 1 | in vitto medil evolution and goldvin. | US-PGPUB; | |
| | | | DERWENT | |
| 5 | 132 | "rna polymerase" and gold.in. | USPAT; | 2003/10/29 12:37 |
| 3 | .132 | Ina porymerase and gord.in. | US-PGPUB; | 2003/10/23 12:37 |
| | | | DERWENT | |
| 6 | 33 | ("rna polymerase" and gold.in.) and | USPAT; | 2003/10/29 12:40 |
| ١٥ | 33 | | US-PGPUB; | 2003/10/29 12.40 |
| | | replicase | | |
| | 0 | (1) (2) (1) (1) (1) (1) (1) (1) (1) (1) (1) | DERWENT | 2003/10/29 12:40 |
| 7 | 0 | ("rna polymerase" and gold.in.) and | USPAT; | 2003/10/29 12:40 |
| | | replicase same pool | US-PGPUB; | |
| | | | DERWENT | 0000/100/00 10 10 |
| 8 | 0 | (("rna polymerase" same (mutation or | USPAT; | 2003/10/29 12:40 |
| | | error)) and (evolution or evolve or | US-PGPUB; | |
| | | selection)) and replicase same pool | DERWENT | |
| 9 | 168 | (replicase same (mutation or error)) and | USPAT; | 2003/10/29 13:00 |
| | | (evolution or evolve or selection) | US-PGPUB; | |
| | | | DERWENT | |
| 10 | 77 | ((replicase same (mutation or error)) and | USPAT; | 2003/10/29 12:41 |
| | | (evolution or evolve or selection)) and | US-PGPUB; | |
| | | target same (evolution or evolve or | DERWENT | |
| l i | | selection) | | |
| 11 | 52 | (((replicase same (mutation or error)) and | USPAT; | 2003/10/29 12:59 |
| | | (evolution or evolve or selection)) and | US-PGPUB; | |
| | | target same (evolution or evolve or | DERWENT | |
| \ | | selection)) not gold.in. | | |
| 12 | 409 | hiv near8 selection | USPAT; | 2003/10/29 12:59 |
| | | | US-PGPUB; | |
| | | | DERWENT | |
| 13 | 89 | (hiv near8 selection) and target near8 | USPAT; | 2003/10/29 13:00 |
| | | selection | US-PGPUB; | |
| | | | DERWENT | |
| 14 | 9249 | (polymerase same (mutation or error)) and | USPAT; | 2003/10/29 13:00 |
| | | (evolution or evolve or selection) | US-PGPUB; | |
| | | | DERWENT | |
| 15 | 102 | (hiv near8 selection) and (polymerase same | USPAT; | 2003/10/29 13:00 |
| | - | (mutation or error)) and (evolution or | US-PGPUB; | |
| | | evolve or selection) | DERWENT | |
| 16 | 34 | ((hiv near8 selection) and target near8 | USPAT; | 2003/10/29 13:01 |
| | ~ 1 | selection) and (polymerase same (mutation | US-PGPUB; | |
| | | or error)) and (evolution or evolve or | DERWENT | |
| | | selection) | 551,111,111 | |
| 17 | 32 | (((hiv near8 selection) and target near8 | USPAT; | 2003/10/29 13:01 |
| * ' | 32 | selection) and (polymerase same (mutation | US-PGPUB; | 2003/10/25 13.01 |
| | | or error)) and (evolution or evolve or | DERWENT | |
| | | selection)) and rna same (evolution or | DELMENT | |
| | | evolve or selection) | | |
| | | ENOTAE OF SETECTION! | L | <u> </u> |

L3 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 2

ACCESSION NUMBER: 1996:71325 BIOSIS DOCUMENT NUMBER: PREV199698643460

TITLE: Why is the polymerase chain reaction resistant to in

vitro evolution?.

AUTHOR(S): Bull, J. J. [Reprint author]; Pease, C. M.

CORPORATE SOURCE: Dep. Zool., Univ. Texas, Austin, TX 78712, USA

SOURCE: Journal of Molecular Evolution, (1995) Vol. 41, No. 6, pp.

1160-1164.

CODEN: JMEVAU. ISSN: 0022-2844.

DOCUMENT TYPE: Article LANGUAGE: English

ENTRY DATE: Entered STN: 27 Feb 1996

Last Updated on STN: 27 Feb 1996

A variety of methods have been developed to amplify DNA and RNA. AB methods vary in their susceptibility to evolve new molecular species differing from the starting template. PCR is exceptionally resistant to in vitro evolution, whereas methods such as Q-beta replicase and 3SR are much less robust. This paper develops some simple mathematical models which suggest that PCR is resistant to in vitro evolution because the reaction controls replication in discrete cycles: fast replication is of little advantage during PCR because the reaction limits fast replicators as well as slow ones to a single copy per cycle. In contrast, continuous (isothermal) reactions, as in the Q-beta replicase reaction, favor fast replicators. The advantage of fast replication is compounded in continuous reactions, because a fast replicator can complete many generations of replication during the time it takes a slow replicator to complete one generation. These models suggest that continuous amplication protocols will never achieve the robustness against in vitro evolution observed with PCR.

(FILE 'HOME' ENTERED AT 10:40:19 ON 29 OCT 2003)

| | FILE 'MED | LINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 10:40:31 ON 29 OCT 2003 |
|----|-----------|---|
| L1 | 561 | 9 S "IN VITRO SELECTION" OR AFFINITY SELECTION OR "IN VITRO EVOLU |
| L2 | 1 | 3 S L1 AND REPLICASE |
| L3 | | B DUP REM L2 (5 DUPLICATES REMOVED) |
| | | E COIA G?/AU |
| L4 | | O S E7 E6 E1 E2 |
| L5 | 8- | 4 S E7 OR E6 OR E1 OR E2 |
| L6 | 1 | 7 S L5 AND (EVOLUTION OR SELECTION) |
| L7 | | B DUP REM L6 (9 DUPLICATES REMOVED) |
| L8 | | 5 S L7 NOT L3 |

| L Number | Hits | Search Text | DB | Time stamp |
|----------|------|------------------------|-----------|------------------|
| 1 | 9 | coia-g\$.in. | USPAT; | 2003/10/29 10:47 |
| | | | US-PGPUB; | |
| | | | DERWENT | |
| 2 | 1 | 2000-039104.NRAN. | DERWENT | 2003/10/29 10:50 |
| 3 | 1 | "5602001." | DERWENT | 2003/10/29 10:52 |
| 4 | 0 | "5602001" and affinity | DERWENT | 2003/10/29 10:53 |
| 5 | 0 | "5602001" and select\$ | DERWENT | 2003/10/29 10:53 |
| 6 | 0 | "5602001" and bind\$ | DERWENT | 2003/10/29 10:53 |

| L Number | Hits | Search Text | DB | Time stamp |
|----------|-------|--|-----------|------------------|
| 1 | 4722 | affinity near10 selection | USPAT; | 2003/10/29 10:30 |
| | | 1 | US-PGPUB; | ĺ |
| | | | DERWENT | |
| 2 | 10118 | bind\$ near10 specific near10 ligand\$ | USPAT; | 2003/10/29 10:33 |
| | | • | US-PGPUB; | |
| 1 | | | DERWENT | |
| 3 | 3728 | replicase | USPAT; | 2003/10/29 10:30 |
| | | - | US-PGPUB; | |
| | | | DERWENT | |
| 4 | 0 | (affinity near10 selection) same (bind\$ | USPAT; | 2003/10/29 10:30 |
| | | near10 specific near10 ligand\$) same | US-PGPUB; | |
| | | replicase | DERWENT | |
| 5 | 176 | (affinity near10 selection) same (bind\$ | USPAT; | 2003/10/29 10:30 |
| ļ. | | near10 specific near10 ligand\$) | US-PGPUB; | |
| | | - | DERWENT | i |
| 6 | 2 | (affinity near10 selection) same replicase | USPAT; | 2003/10/29 10:32 |
| | | | US-PGPUB; | |
| | | | DERWENT | [|
| 8 | 1 | (bind\$ near10 specific near10 ligand\$) | USPAT; | 2003/10/29 10:32 |
| | | same replicase | US-PGPUB; | |
| | | | DERWENT | |
| 9 | 2905 | vitro near10 selection | USPAT; | 2003/10/29 10:33 |
| | | | US-PGPUB; | |
| | | | DERWENT | |
| 10 | 4 | (vitro near10 selection) same replicase | USPAT; | 2003/10/29 10:34 |
| | | | US-PGPUB; | |
| | | | DERWENT | |
| 11 | . 2 | taussing-\$.in. | USPAT; | 2003/10/29 10:35 |
| | | | US-PGPUB; | |
| | | | DERWENT | |
| 12 | 13885 | (affinity near10 selection) or (bind\$ | USPAT; | 2003/10/29 10:35 |
| | | near10 specific near10 ligand\$) | US-PGPUB; | |
| | | | DERWENT | |
| 13 | 3026 | ((affinity near10 selection) or (bind\$ | USPAT; | 2003/10/29 10:35 |
| | | near10 specific near10 ligand\$)) and "RNA | US-PGPUB; | |
| | | polymerase" | DERWENT | 0000/10/00 10 05 |
| 14 | 13 | ((affinity near10 selection) or (bind\$ | USPAT; | 2003/10/29 10:35 |
| | | near10 specific near10 ligand\$)) near10 | US-PGPUB; | |
| | | "RNA polymerase" | DERWENT | <u></u> |